Short Term Effects of Mild Severity COVID-19 on Left Ventricular Functions

Osman Bektaş (bektas7960@gmail.com)
Ordu Üniversitesi Tıp Fakültesi https://orcid.org/0000-0002-6616-9891
Ahmet Karagöz
Giresun University Faculty of Medicine: Giresun Universitesi Tip Fakultesi
Feyza Nur Topçu Yenerçağ
Provincial Health Directore
Seçkin Dereli
Ordu University Faculty of Medicine: Ordu Universitesi Tip Fakultesi
Celali Kurt
Ordu University Faculty of Medicine: Ordu Universitesi Tip Fakultesi
Yasemin Kaya
Ordu University Faculty of Medicine: Ordu Universitesi Tip Fakultesi

Research Article

Keywords: Covid-19, Subclinical left ventricular dysfunction, Speckle tracking echocardiography

Posted Date: September 20th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-869751/v1

Abstract

Purpose: We aimed to evaluate long term effects of COVID-19 disease on left ventricular function using speckle tracking echocardiography.

Methods: In our study, 96 non-hospitalized patients who were diagnosed with COVID-19 disease in our center between 15 August 2020 and 01 September 2020 and 96 age and gender matched control subjects were included.

Results: The mean follow up duration was 137 ± 7 days. White blood cell, neutrophile and lymphocyte were significantly lower and C-reactive protein (CRP) and neutrophil to lymphocyte ratio (NLR) were significantly higher in the COVID-19 group. (6.6 ± 2.8 vs. 24.4 ± 21.8, p <0.001 and 4.1 ± 2.5 vs. 7.1 ± 4, p <0.001, respectively). LV-GLS and LV-GCS were significantly lower in the COVID-19 group. (-20.1 ± 3.1 vs -15.9 ± 2, p <0.001 and -29.3 ± 2.1 vs -26.3 ± 2.1, p <0.001, respectively). LV-GLS and LV-GCS were found to be negatively correlated with CRP (rs = -0.515, p <0.001 and rs = 0.-466, p <0.001, respectively) and NLR (rs = -0.494, p <0.001 and rs = -434, p <0.001, respectively).

Conclusion: Deteriorating effects of COVID-19 disease on both LV-GCS and LV-GLS can be seen even in the short term. These detrimental effects seem to be associated with CRP levels and NLR measured in the course of active infection.

Introduction

COVID-19 disease, which was firstly identified in Wuhan, China in December 2019, is an infectious respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1] Currently, the world is still under the influence of the disease, which later on turned into a pandemic. [2]

In addition to lung involvement in the form of interstitial pneumonia, multiorgan failure can develop in more severe cases. Along with respiratory system involvement, it has been found that cardiovascular and mental disorders are also seen during the course of COVID-19 infection[3]. Previous reports have revealed myocardial damage in 20–40% of COVID-19 cases hospitalized due to cardiac chest pain, fulminant heart failure, cardiac arrhythmias and cardiac arrest[3]

Conventional echocardiographic assessment may sometimes be insufficient for evaluation of global ventricular systolic function. Studies showed that left ventricular systolic function which appears to be normal with traditional echocardiographic methods, can be found to be deteriorated in speckle tracking echocardiographic (STE) imaging[4]. Echocardiographic imaging techniques enable more quantitative evaluation of complex ventricular movements[5]. Among these imaging techniques, speckle tracking is an operator and angle independent method for evaluating regional and global wall movements and is more sensitive in detecting subclinical right and left ventricular dysfunction [6]. In a very recent study, left ventricular global longutinal strain (LV-GLS) was found to be affected by COVID-19 infection. Furthermore, it was found to be an independent predictor of mortality in COVID-19 patients[7].

In this study we aimed to investigate possible subtle changes in left ventricular systolic function in patients with COVID 19 disease using STE and determine whether the improvement in clinical and laboratory findings is accompanied by cardiac improvement in the long term.

Material And Method

This cross-sectional, single-centre study was performed in University of Ordu Training and Research Hospital, which was determined to treat COVID-19 patients by Turkish Republic Ministry of Health, between November 15 August 2020 and 01 September 2020. The mild severity COVID-19 patients; was defined as patients who were followed outpatient, non-hospitalized, and who had constituional symptoms including fever, muscle and / or joint pain, cough, sore throat, without respiratory distress (respiratory rate <24/minutes, peripheral capillary oxigen saturation (SpO2) > 93% at room) according to the World Health Organization and the Republic of Turkey Ministry of Health COVID-19 Treatment Guidelines . 120 patients with mild severity COVID-19 disease who were older than 18 years old and treated with only hydroxychloroquine and/or favipiravir were respectively enrolled in the study. Patients with systolic heart failure (LVEF ≤ 50%), coronary artery disease, chronic inflammatory disease, hypertension, severe chronic renal and liver failure, right or left ventricular failure, atrial fibrillation, complete or incomplete branch block, moderate-severe valve pathology, pacemaker, anemia, chronic renal failure, thyroid dysfunction, pulmonary embolism, cancer, chronic lung disease, body mass index (BMI) > 30 kg/m^2 were excluded. In addition, patients who were given steroids and/or heparin treatments along with hydroxychloroquine and/or favipiravir due to COVID-19 and those who had any other active infection disease and used antibiotics and poor echocardiographic images were excluded. After the exclusion criterias were applied, the study continued with 96 mild severity COVID-19 patients. Age and sex matched 96 healthy individuals forming the control group were selected consecutively from the outpatient clinic. Demographic data, baseline characteristics, medical history, drugs and medications used for COVID-19, smoking habits and laboratory values were obtained using the hospital's medical database. Laboratory parameters including; complete blood count (CBC), C - reactive protein (CRP), D-dimer, ferritin, cardiac troponin I (cTnI) and other biochemical parameters were measured at the first admission to the hospital before COVID-19 treatment started. The entire study population were evaluated via two-dimensional echocardiography and speckle tracking echocardiographic imaging. The COVID-19 patients' echocardiographic examinations were performed average 4.5 (3-6 months) months after COVID-19 diagnosis. The research procedures were revised and approved by the local hospital's ethics committee and Ministry of Health Scientific Research Platform (No: 2020-11-07T18_44_00) according to the ethical considerations stipulated in the Helsinki Declaration.

Diagnosis of COVID-19

According to the World Health Organization and the Republic of Turkey Ministry of Health according to the COVID-19 Treatment Guidelines, patients who were matching the definition of probable SARS-CoV-2 infection case underwent testing with molecular methods to scan for viruses. Throat and nasopharynx swab samples were collected from all patients in our study to extract SARS-CoV-2 RNA. Real-time reverse

transcription polymerase chain reaction assay (RT-PCR) molecular method was applied for RNA analysis of SARS-CoV-2 virus. Cases with SARS-CoV-2 RNA in RT-PCR method were accepted as COVID-19.

Two-dimensional echocardiography (2DE)

Conventional 2D echocardiographic examination was performed using a commercially available echocardiography device (EPIQ 7C; Philips Medical Systems, Andover, Massachusetts) in line with the recommendations of the American Echocardiography Association[8] . All these echocardiographic examinations were performed by experienced two operators. Echocardiographic examinations were performed in left lateral decubitus position after resting for at least 15 min. Blood pressures of the study population were measured prior to echocardiographic examination; right arm average systolic blood pressure was measured 118.5 mmHg / diastolic blood pressure was measured 78.5 mmHg, left arm average systolic blood pressure was measured 120.5 mmHg / diastolic blood pressure was measured 80.5 mmHg. All measurements were taken in three consecutive cycles, and average values were calculated. Patients with optimal views of left ventricul for STE analysis were included in the study. 12 patients were excluded due to poor echocardiographic images. The patients were monitored by electrocardiogram throughout the procedure. Left ventricle (LV) and left atrium (LA) diameters and LV wall thicknesses were measured from parasternal long axis views by M-mode echocardiography. Left ventricular ejection fraction (LVEF) was calculated from the apical 4-chamber and 2-chamber images using the Modified Simpson method[9]. Pulsed vawe Doppler velocity recordings were obtained in apical four-chamber images via placing the sample volume at the tips of the mitral valve.

E/A ratio was calculated following assessment of mitral early peak velocity (E) and mitral late peak velocity (A). Stroke volume (EDV—ESV, ml) and cardiac output (stroke volume x heart rate, l/m) were driven after calculation of LV end-diastolic volume (LV EDV, ml) and end-systolic volume (LV ESV, ml). Tricuspid regurgitation peak velocity was used for measurement of systolic pulmonary artery pressure (sPAP). Devereux formula was used to calculate the LV mass [10]. Finally, all measurements were re-analysed considering the body mass index (BMI).

Speckle Tracking Echocardiography

The myocardial deformation quantitative analysis function of 2D-STE was used to evaluate myocardial function. The end of systole was defined as the time at which the aortic valve is closed and the end of diastole was defined as the peak R wave in the electrocardiogram. Endocardial borders were monitored within the frame of 2D images at the end of systole. A wide myocardial width was adjusted to determine the epicardial border. Automatic function was used to determine the midpoints between the endocardial and epicardial borders and the middle myocardial border. In order to ensure correct tracking and to involve all LV wall thickness for 2D speckle viewing width, manual adjustment was performed when necessary. Apical four-, three-, and two- chamber views were used for evaluation of LV-GLS.

All images used for speckle-tracking echocardiographic analysis were obtained using the QLAB-CMQ software program Philips Epiq 7C at a frame rate of 50 to 70 fps. Peak systolic strain measurements of

each segment were automatically taken by a software (analysis) program. Following assessment of longitudinal strain values of a total of 18 segments, the mean value was determined as the global strain[11] (Figure 1). The circumferential strain used to evaluate myocardial shortening/ lengthening along the LV curvature was measured from the LV mid-ventricular short-axis view. The global circumferential strain was calculated from the average peak systolic strain value of six segments. Negative values were used to determine global longitudinal and circumferential strains, and less negative values indicated lower strains. (Figure 2).

Statistical analyses

In all statistical analysis SPSS 22.0 Statistical Package Program for Windows (SPSS Inc., Chicago, IL, USA)was used. In order to test normality of distribution Kolmogorov–Smirnov test was used. Quantitative variables were specified as the mean ± standard deviation. Categorical variableswere shown as number and percentage values. Differences between groups were evaluated by using Student's t-test andMann Whitney U test. Categorical variables were compared with Chi-square test. Spearman correlation analysis was performed to examine the relationship between LV GCS, LV GLS and NLR, CRP. A p value of <0.05 was accepted as statistically significant.

Results

A total of 96 patients who had recovered from COVID-19 disease and 96 healthy controls were included in the study. The mean follow-up duration in the patient group was 137 ± 7 days. The mean age was similar in the COVID-19 and control groups. (43.4 ± 12.8 vs. 44.3 ± 13.1, $p = 0.590$, respectively). There was no statistically significant difference between the groups in terms of gender, BMI, heart rate, diabetes, hypertension and smoking status. White blood cell, neutrophil and lymphocyte were significantly lower in the COVID-19 group. On the other hand, C-reactive protein levels and NLR were significantly higher in the COVID-19 group. (2.6 ± 1.8 vs. 24.4 ± 20.1, $p < 0.001$ and 4.1 ± 2.5 vs. 7.1 ± 4, $p < 0.001$, respectively). Average levels of C - reactive protein (CRP), ferritin and D-dimer were higher than normal values in only patients with COVID-19. cTnI level was higher than normal values in only three patients with COVID-19. The baseline characteristics and laboratory findings of the study population are summarized in Table 1.

Table 1
Comparision of baseline characteristics and laboratory findings between COVID-19 and control groups

Parameters	Control (n = 96)	COVID-19 (n = 96)	p value
Age, years	43.4 ± 12.8	44.3 ± 13.1	0.590
Gender, male, n (%)	45 (46.8)	43 (44.7)	0.772
Body mass index, kg/m^2	24.8 ± 2.1	24.2 ± 2.5	0.145
Hypertension, n (%)	21 (21.6)	18 (18.7)	0.590
Diabetes mellitus, n (%)	14 (14.5)	12 (12.1)	0.673
Hyperlipidaemia, n (%)	9 (9.3)	10 (10.4)	0.549
Smoking, n (%)	47 (48.9)	42 (43)	0.469
White blood cell, 10^3 uL	6.4 ± 1.6	7.8 ± 3.2	**0.004**
Neutrophil, 10^3 uL	4.2 ± 2.2	5.5 ± 2.3	**< 0.001**
Lymphocyte, 10^3 uL	1.1 ± 0.4	0.8 ± 0.3	**< 0.001**
Monocyte, 10^3 uL	0.59 ± 0.3	0.61 ± 0.3	0.634
Platelet, 10^3 uL	233 ± 77	244 ± 81	0.289
Hemoglobin, g/dl	13.1 ± 1.6	12.7 ± 1.7	0.113
Glucose, mg/dl	97.0 ± 8.5	95.5 ± 9.2	0.516
Aspartate aminotransferase, IU/l	29.9 ± 7.6	27.9 ± 9.7	0.348
Alanine aminotransferase, IU/l	29.5 ± 9.4	28.2 ± 15.5	0.485
Creatinin mg/dl	0.87 ± 0.22	0.86 ± 0.23	0.469
Sodium, mEq/L	137 ± 3	137.1 ± 3.1	0.611
Calcium, mg/dl	9.40 ± 0.55	9.45 ± 0.57	0.619
Potassium, mmol/L	4.2 ± 0.3	4.1 ± 0.3	0.203
cTnI, ng/mL	N.A.	0.534	N.A.
Hydroxychloroquine, n (%)	N.A	19 (19.7)	N.A.
Favipiravir, n (%)	N.A	77 (80.3)	N.A.

Data are given as mean ± SD, (%), maximum and minimum. cTnI: Cardiac troponin I; N.A.: Not applicable

Parameters	Control (n = 96)	COVID-19 (n = 96)	p value
Hydroxychloroquine and Favipiravir, n (%)	N.A.	19 (19.7)	N.A.
C - reactive protein, mg/L	2.6 (0–3)	24.4 (46–3)	**< 0.001**
Neutrophil to lymphocyte ratio	4.1 ± 2.5	7.1 ± 4	**< 0.001**
D-dimer, ng/mL	N.A.	340 ± 190	N.A.
Ferritin, ng/mL	N.A.	208 ± 98	N.A.
Data are given as mean ± SD, (%), maximum and minimum. cTnI: Cardiac troponin I; N.A.: Not applicable			

When conventional 2D echocardiographic findings were compared, LVEF, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), left ventricular septal wall thickness (LVSWT), posterior wall thickness (PWT), left ventricular mass index (LVMI) and left atrium diamater were similar between two groups (Table 2).

Table 2
Comparision of electrocardiographic and echocardiographic findings between COVID-19 and control groups

Parameters	Control (n = 96)	COVID-19 (n = 96)	p value
Heart rate, bpm	78.7 ± 8	77.2 ± 6	0.301
LVEF, %	62.5 ± 1.4	62.7 ± 1.2	0.216
LVESD, mm	36.1 ± 1.9	35.5 ± 2.3	0.125
LVEDD, mm	45.2 ± 16.3	45.1 ± 2.3	0.783
LVSWT, mm	10.2 ± 0.7	10 ± 0.6	0.264
PWT, mm	9.2 ± 0.5	9 ± 0.6	0.207
LVMI, g/m^2	73.4 ± .4	74.2 ± 3.7	0.484
LAD, mm	35.8 ± 2.2	36.2 ± 2.6	0.339
Average E/e' ratio	10.7 ± 1.1	10.1 ± 1.1	0.770
sPAP, mmHg	23.4 ± 2.4	24.1 ± 2.5	0.520
LV GLS, %	-20.1 ± 3.1	-15.9 ± 2	**< 0.001**
LV GCS, %	-29.3 ± 2.1	-26.3 ± 2.1	**< 0.001**

Data are given as mean ± SD or (%), Bpm: beats per minute; LVEF: Left ventricular ejection fraction; LVEDD: Left ventricular end-diastolic diameter, LVESD: Left ventricular end-systolic diameter LVSWT : Left ventricular septal wall thickness, PWT : Posterior wall thickness, LVMI : Left ventricular mass index LAD : Left atrium diamater, sPAB: Systolic pulmonary arterial pressure, LV: Left ventricular, GLS: Global longitudinal strain, GCS: Global circumferential strain,

LV-GLS and LV-GCS values were significantly lower in the COVID-19 group when compared to controls. (-20.1 ± 3.1 vs. -15.9 ± 2, $p < 0.001$ and − 29.3 ± 2.1 vs. -26.3 ± 2.1, $p < 0.001$, respectively). (Table 2). Spearman correlation analysis showed that there was a statistically significant negative correlation between LV-GLS and LV-GCS values and CRP levels ($rs = -0.515$, $p < 0.001$ and $rs = 0.-466$, $p < 0.001$, respectively) (Fig. 3A, 3B) as well as NLR ($rs = -0.494$, $p < 0.001$and $rs = -434$, $p < 0.001$, respectively). (Fig. 4A, 4B) .Left ventricular systolic function was found to be similarly affected in both men and women. LV GLS − 15.7 ± 2.1 vs.-15.9 ± 2, $p = 0.498$, LV GCS − 26.1 ± 2.1 vs -26.2 ± 2.0 $p = 0.646$

Discusssion

Our study results revelaed that LV-GLS and LV-CLS values were decreased in patients who had recovered from COVID-19 disease, when compared to controls. Moreover, these decreased values had a significant negative correlation with C-reactive protein (CRP) levels and neutrophil lymphocyte ratio (NLR), which are inflammatory markers showing the severity of the disease during the active infection. The long term

subclinical deterioration in left ventricular systolic function indicates that even recovered COVID-19 infection may have prolonged cardiac effects.

The novel coronavirus COVID-19 outbreak, first reported on December 8 2019 in Hubei province of China, was recognized as a pandemic by the World Health Organization (WHO) on March 11, 2020. Now available data in public databases, signifies that the infection and mortality risk increases in men and elderly individuals [3]. However, in our study, left ventricular systolic function was found to be similarly affected in both men and women.

Systematic inflammation, pro-inflammatory cytokine storm and sepsis resulting in multiorgan failure and death can be seen in severe COVID-19 disease [12]. Cardiac arrhythmia is also an expected finding in COVID-19 disease and the possible pathophysiologic mechanisms are metabolic dysfunction, myocardial inflammation, and activation of the sympathetic nervous system [13]. Following Acute Respiratory Distress Syndrome (ARDS), arrhythmia is the second most common clinical finding in severe COVID-19 disease and was detected in 16.7% of the patients. The frequency of arryhthmia was 7% in patients who did not require ICU treatment and 44% in those who were admitted to the ICU [14]. Atrial fibrillation, conduction block, ventricular tachycardia, and ventricular fibrillation were the most common arrhythmia types.

Fulminant myocarditis is one of the catastrophic cardiac complications of COVID-19 disease. Heart failure was reported in 23% of COVID-19 patients in a recent report in China. Reports, heart Heart failure was evident in 12% of the survivors and in approximately 52% of those who lost their lives[15]. In a another study, LV-GLS was found to be impaired even in patients who did not have a severe COVID-19 disease and had relatively low troponin levels[7]. Subtle myocardial deterioration was defined as a predictor of death in COVID-19 disease. Therefore, LV longitudinal strain was adopted to be a precise predicion tool for COVID-19 disease considering its early and more robust detection capacity compared to conventional echocardiography [7].

The Neutrophile-Lymphocyte ratio (NLR) can be calculated simply by dividing the absolute neutrophile count by the lymphocyte count. The increase in NLR is valuable in terms of reflecting the general inflammatory status of the patient[16]. It has been reported that neutrophils are the first inflammatory cells to migrate to ischemic myocardial tissue, and they inflict damage via proteolytic enzymes, reactive oxygen radicals and by stimulating secretion of the other neutrophils[17]. Inflammation is known to be the starting point for all cardiovascular disorders. NLR has been reported to be in a strong relationship with cardiovascular diseases in many epidemiological studies[18]. The main reason for this is that NLR consists of two separate inflammation markers. It is well known that especially severe cases of COVID 19 have a higher rate of NLR[19]. In a study including 245 hospitalized patients, NLR was identified as an independent predictor of in-hospital mortality for COVID-19 disease[20]. In our study, the relationship between LV-GLS and LV-GCS values and CRP levels as well as NLR supports the hypothesis that active inflammation is an indicator of long term cardiac outcomes. Based on these findings, it can also be

speculated that evaluation of NLR during the active course of the disease may be helpful in identifying the individuals with high cardiac risk.

High levels of lactate dehydrogenase (LDH), serum creatine kinase (CK), and CRP were detected in patients with COVID-19 disease [21]. Moreover high CRP level was positively correlated with lung lesions in the early stage and reflected severity of COVID-19 disease [22]. Another study revealed that CRP levels increase significantly and predict severe COVID-19 disease even before findings are detected in lung computerized tomography (CT) imaging[23]. These studies emphasize the prognostic value of CRP levels in COVID-19 disease.

We speculate that, the reasons for subclinical deterioration in LV systolic function even after an average of 4.5 months following active disease may be the delay in healing of COVID-19 myocarditis and/or the damage caused by the inflammation itself in the acute period. The negative correlation between increasing levels of CRP levels and NLR and decreasing LV-GLS and LV-CS values seem to support this hypothesis. However, longer-term follow-up is needed to monitor how long the cardiac effect will continue or whether it will be permanent.

Limitations

Single center design, small sample size and short follow up can be considered as the limitations of our study. Other inflammatory markers such as interleukin-6 and erythrocyte sedimentation rate could also be evaluated. Lack of data about myocardial function before COVID-19 disease can hinder interpretation of our outcomes. Comorbidities and medications used are possible confounders for strain measurements. Finally addition of a confirmation method for evaluation of myocardial impairment such as magnetic resonance imaging would strengthen the scientific power of our study.

Consequently, both LV-GCS and LV-GLS were found to be decreased in patients with COVID-19 disease in the long term. This decrease is associated with the increase in CRP levels and NLR. Since subclinical LV systolic dysfunction can not be detected by conventional echocardiographic assessment, we believe in the necessity of STE to evaluate left ventricular systolic function in COVID-19 patients in the long term. Close follow-up of the patients with subclinical LV systolic dysfunction may be reasonable in terms of preventing more severe cardiac complications.

Declarations

Conflict of interest

The authors declare that they have no conflict of interest.

References

1. Peeri, N.C, Shrestha, N. Rahman, M.S. Zaki R, et al. U. (2020), “The SARS, MERS and Novel Coronavirus (COVID-19) Epidemics, The Newest and Biggest Global Health Threats: What Lessons Have We Learned? International Journal of Epidemiology, 1: 1-10.
2. Lee KY, Lee BK, Kim WJ, et al; Korean Society of Interventional Cardiology COVID-19 Task Force Team. Consensus Statement on Coronary Intervention during the Coronavirus Disease 2019 (COVID-19) Pandemic: from the Korean Society of Interventional Cardiology (KSIC). Korean Circ J. 2020 Nov;50(11):974-983.
3. Tomasz J Guzik, Saidi A Mohiddin, Anthony Dimarco, et al. COVID-19 and the Cardiovascular System: Implications for Risk Assessment, Diagnosis, and Treatment Options. Cardiovasc Res. 2020 Apr 30;cvaa106.
4. Cascino GJ, Voss WB, Canaani J, et al. Two-dimensional speckle-tracking strain detects subclinical cardiotoxicity in older patients treated for acute myeloid leukemia. Echocardiography. 2019 Nov;36(11):2033-2040.
5. Mombeini H, Parsaee M, Amin A. Speckle tracking echocardiography in hypokinetic non-dilated cardiomyopathy: comparison with dilated cardiomyopathy. ESC Heart Fail. 2020 Aug;7(4):1909-1916.
6. Biswas M, Sudhakar S, Nanda NC,et al. Two- and three-dimensional speckle tracking echocardiography: clinical applications and future directions. Echocardiography. 2013 Jan;30(1):88-105.
7. Baycan OF, Barman HA, Atici A, et al. Evaluation of biventricular function in patients with COVID-19 using speckle tracking echocardiography. Int J Cardiovasc Imaging. 2020 Aug 15:1–10.
8. Mitchell C, Rahko PS, Blauwet LA, et al (2019) Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr. J Am Soc Echocardiogr. 2019 Jan;32(1):1-64.
9. Yenerçağ M, Yüksel S, Çoksevim M, et al. Noninvasive cardiac output measurement based optimization in nonresponders of cardiac resynchronization therapy. Pacing Clin Electrophysiol. 2020 Apr;43(4):394-401.
10. de Simone G, Daniels SR, Devereux RB, et al. Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight. J Am Coll Cardiol. 1992 Nov 1;20(5):1251-60.
11. Cerqueira MD, Weissman NJ, Dilsizian V, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: a statement for healthcare professionals from the cardiac imaging committee of the council on clinical cardiology of the American Heart Association. Circulation 2002 Jan 29;105(4):539-42.
12. Iwata-Yoshikawa N, Okamura T, Shimizu Y, et al. TMPRSS2 contributes to virus spread and immunopathology in the airways of murine models after coronavirus infection. J Virol 2019;93:e01815–18.

13. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020 Mar 17;323(11):1061-1069. .
14. Liu K, Fang YY, Deng Y, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J (Engl). 2020 May 5;133(9):1025-1031.
15. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054–1062.
16. Liu Y, Du X, Chen J, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. J Infect. 2020 Jul;81(1):e6-e12.
17. Williams BA, Merhige ME. Association between neutrophil-lymphocyte ratio and impaired myocardial perfusion in patients with known or suspected coronary disease Heart Lung. 2013;42(6):436-41.
18. Adamsson Eryd S, Smith JG, Melander O, et al. Incidence of coronary events and case fatality rate in relation to blood lymphocyte and neutrophil counts. Arterioscler Thromb Vasc Biol. 2012;32(2):533-9.
19. Qin C, Zhou L, Hu Z, et al. Dysregulation of Immune Response in Patients With Coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis. 2020 Jul 28;71(15):762-768.
20. Liu Y, Du X, Chen J, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. J Infect. 2020 Jul;81(1):e6-e12.
21. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.
22. Wang L. C-reactive protein levels in the early stage of COVID-19. Med Mal Infect. 2020 Jun;50(4):332-334.
23. Tan C, Huang Y, Shi F, et al. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. J Med Virol. 2020 Jul;92(7):856-862.

Figures

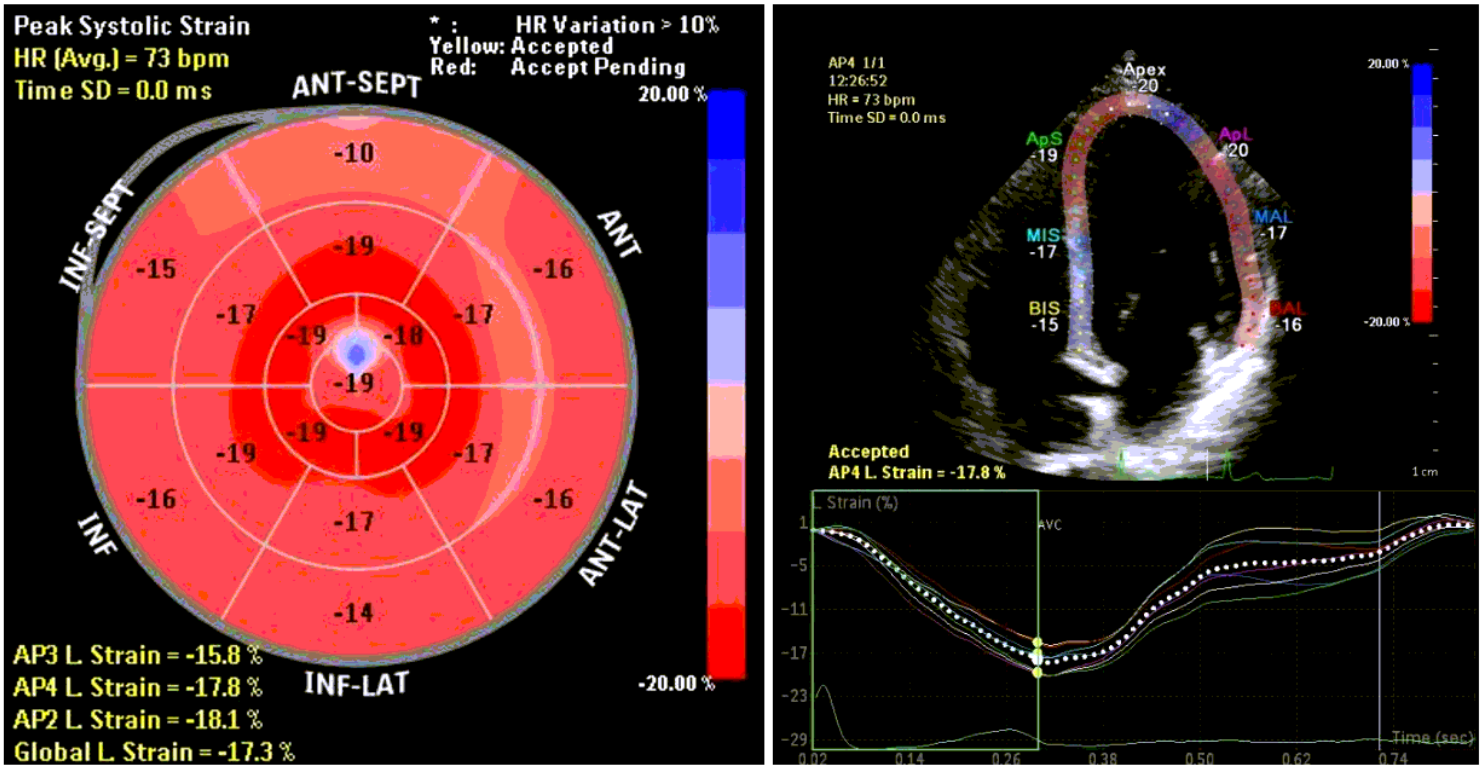

Figure 1

Bull's eye images of left ventricular longitudinal strain (LV-GLS) values of Covid-19 patients

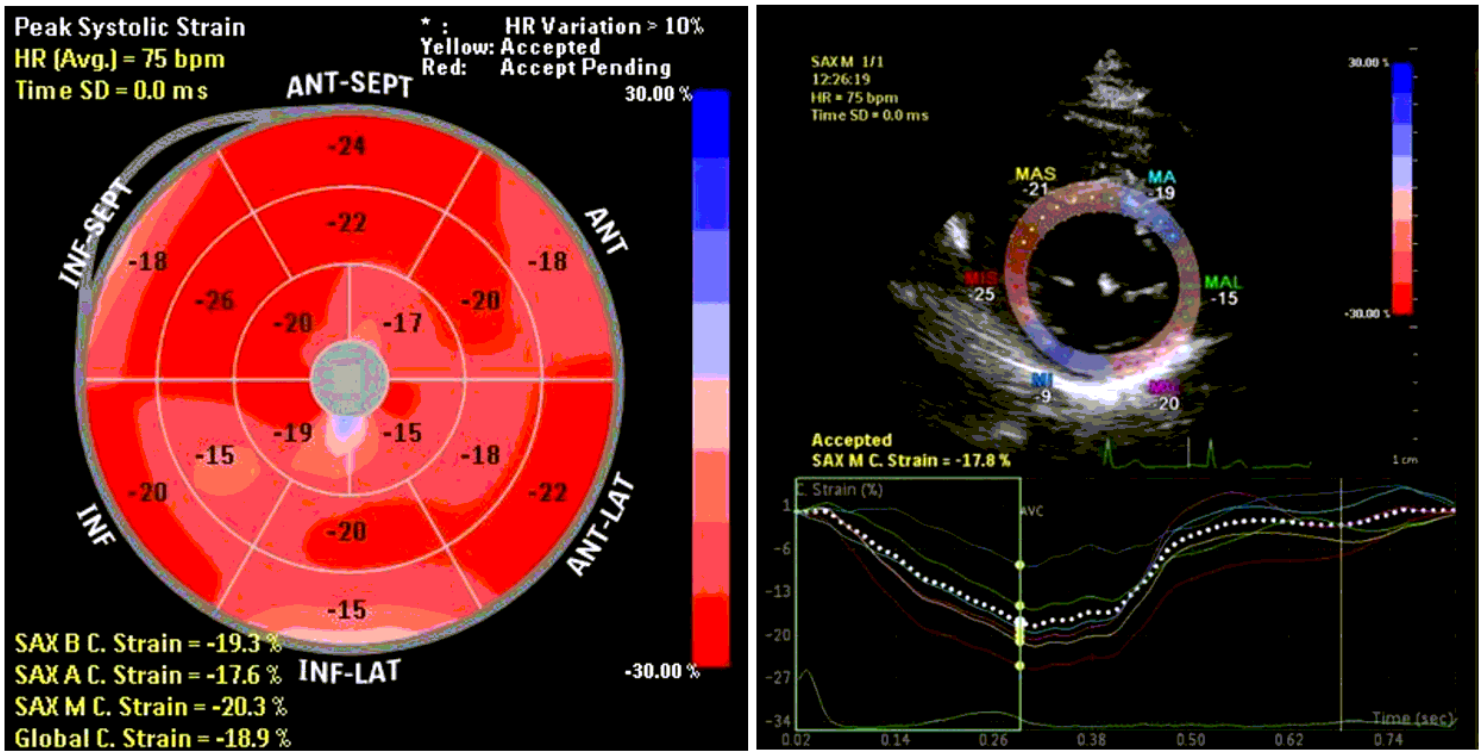

Figure 2

Bull's eye images of left ventricular circumferential strain (LV-GCS) values Covid-19 patients

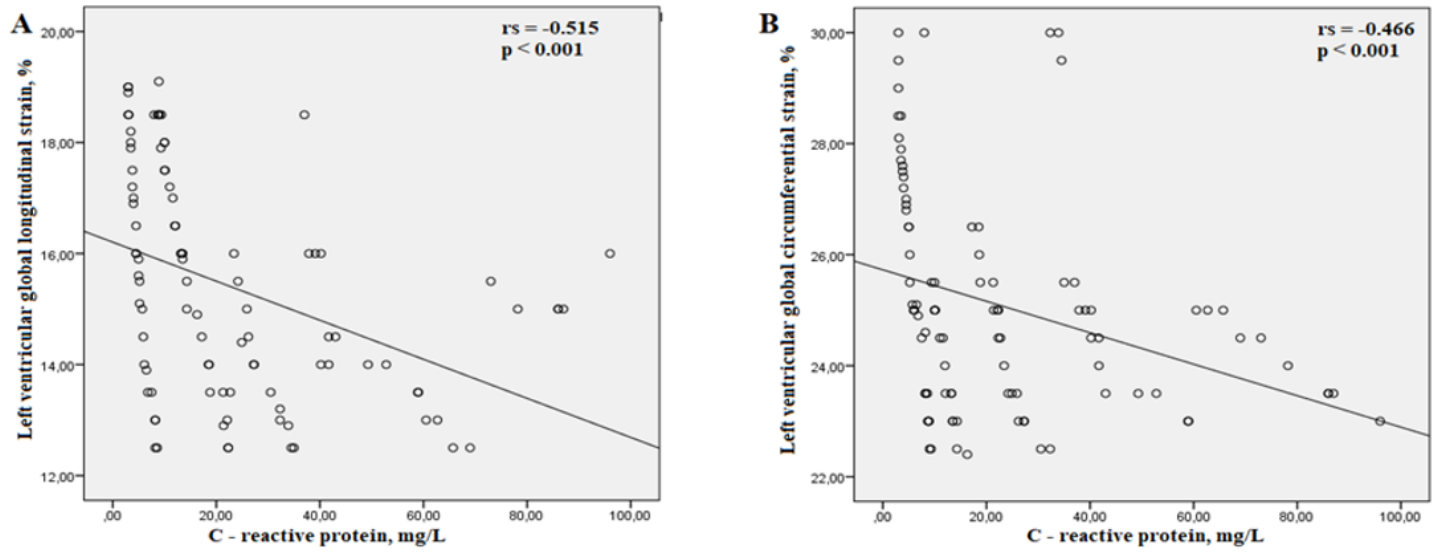

Figure 3

(A) Correlation between LV GLS and CRP. (B) Correlation between LV GCS and CRP

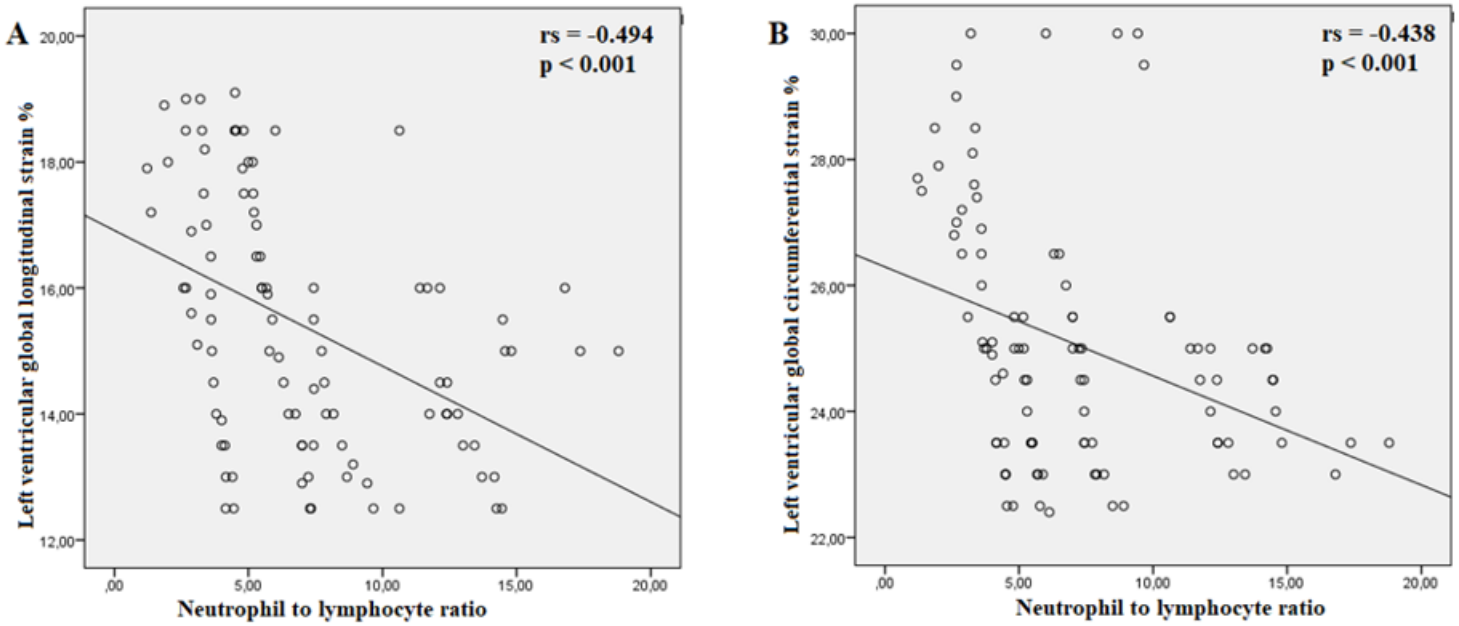

Figure 4

(A) Correlation between LV GLS and NLR. (B) Correlation between LV GCS and NLR.